## REMARKS

Applicants appreciate the examination of the present application as evidenced by the Office Action dated October 27, 2009 (hereinafter, "the Office Action"). Claims 2-9, 13, and 15-23 are currently pending in the present application. Applicants further appreciate the Examiner's willingness to participate in a telephone interview to discuss the present application, which telephone interview is discussed further below.

Applicants respectfully request further consideration of the application in view of the amendments presented herein and the comments that follow to address the issues raised in the Office Action.

### I. Interview Summary

During the telephone interview on December 23, 2009, the Examiner, Applicants' legal representative Dr. Shawna Cannon Lemon and inventor Barry J. Maurer, M.D., Ph.D. discussed compositions described in U.S. Patent No. 4,874,795 to Yesair, U.S. Patent No. 5,972,911 to Yesair, U.S. Patent No. 4,665,098 to Gibbs et al. and the present application. As summarized in the Interview Summary dated December 31, 2009, Applicants discussed the shortcomings of the conventional formulations and distinguished the conventional formulations from the compositions recited in the pending claims.

The present Amendment is submitted to present claim amendments and further remarks consistent with those discussed during the telephone interview in order to reduce the outstanding issues, and it is Applicants' belief, to place the application in condition for allowance.

### II. Doubling Patenting

Applicants acknowledge that the Examiner has maintained the nonstatutory obviousness-type double patenting rejection. Applicants understand and appreciate the Examiner's position stating that the rejection will continue to be made until the rejection is overcome. However, Applicants respectfully submit that Applicants will provide a terminal disclaimer, if still deemed necessary, upon the indication of allowable subject matter.

## III. Claim Rejections Under 35 U.S.C. §103

Claims 2-9, 13 and 15-23 remain rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,352,844 to Maurer et al. (hereinafter, "Maurer et al.") in view of U.S. Patent No. 4,874,795 to Yesair (hereinafter, "Yesair I") or U.S. Patent No. 5,972,911 to Yesair (hereinafter, "Yesair II") and further in view of U.S. Patent No. 4,665,098 to Gibbs et al. (hereinafter,"Gibbs et al.") and U.S. Patent No. 4,327,116 to Weith (hereinafter, "Weith"). *See* Office Action, page 4.

More specifically, the Office Action states the following:

> Claim 15 is amended to say that the flowable powder comprises retinide and the excipients recited. But, Gibbs teaches fenretinide composition that comprises fenretinide or retinide, corn oil, non-ionic surfactant and that the composition can be delivered by mixing in food, spread on bread or crackers of by filing the composition in a soft or hard gelatin capsule, and can also be delivered in powdered form. Thus, the composition of Maurer in combination with Yesair I or Yesair II and Gibbs in the form of a powder would also contain all the components of the composition including the excipients as according to the composition of Maurer in view of Yesair.

Office Action, page 6 (citations omitted).

> Applicant is of the view that amending claim 15 to say that the dry flowable powder contains (a)-(d) overcomes the art, but because fenretinide has been contemplated to be delivered as a powder, then the composition of Maurer in view of Yesair I or II in powder form also contains the excipients disclosed by the combined references.

Office Action, page 7.

For reasons made of record previously, Applicants respectfully submit that the cited references neither alone nor in combination teach or suggest the presently claimed invention. In furtherance of the telephone interview with the Examiner and the Interview Summary prepared by the Examiner regarding the same, Applicants direct the Examiner's attention to a further distinction. Namely, Applicants respectfully submit that none of the cited references teach or suggest the use of flour and a sweetener in a dry flowable powder composition as recited in the pending claims directed to embodiments of the present invention. In addition to

improving the taste of the desired product providing a significant improvement over the products of the cited references, the present invention further allows an improvement of clinical significance.

As noted previously, a composition of the present invention obtained much higher plasma and tissue levels than did the Gibbs formulation at equivalent doses. Further, the compositions comprising the flour and sweetener components obtained higher drug levels in plasma and brain than did fenretinide as formulated in the Gibbs corn oil capsules. Applicants respectfully submit that the corresponding data to support this finding was submitted in a Declaration Under 37 C.F.R. §1.132 of Barry J. Maurer, M.D., Ph.D. (hereinafter, "the Maurer Declaration"), which accompanied Applicants' Amendment After Final Response submitted August 13, 2009. A copy of the Maurer Declaration is resubmitted herewith for the Examiner's convenient reference.

Applicants specifically direct the Examiner's attention to Point 5 of the Maurer Declaration, and Appendix 7 of the Maurer Declaration presenting the journal article titled "Improved oral delivery of N-(4-hydroxyphenyl)retinamide with a novel LYM-X-SORB organized lipid complex." Clin Cancer Res, 13(10):3079-3086, (2007), and more specifically, page 3080 of the journal article. There, it is stated that this new formulation, as recited in the pending claims, "obtained significantly higher plasma and tissue levels in mice than did an equivalent dose of fenretinide delivered using the contents of the corn oil capsule. We also report that the 4-HPR/LYM-X-SORB oral powder prolonged survival in two of three human neuroblastoma murine xenograft models." The results are presented graphically in Figures 1 and 2 on pages 3080 and 3081 of the journal article.

Additionally, the compositions as recited in the pending claims can be provided to patients with relapsed neuroblastoma and can be used to achieve higher plasma levels than equivalent fenretinide doses previously delivered using corn oil capsules. Corresponding data to support this finding is submitted herewith in a second Declaration Under 37 C.F.R. §1.132 of Barry J. Maurer, M.D., Ph.D. (hereinafter, "the second Maurer Declaration"). As shown in the figure provided at Appendix 2 of the second Maurer Declaration, an embodiment of the present invention, fenretinide/LXS oral powder, attained several-fold higher fenretinide

plasma levels (peak and trough) compared to equivalent doses of fenretinide previously delivered using corn oil capsules on similar dosing schedules. Of further clinical significance, the fenretinide/LXS oral powder scored more Complete Responses (%) in neuroblastoma tumor than when using the corn oil capsules as shown in the table at Appendix 4. Thus, Applicants respectfully submit that obtaining higher drug levels in the blood plasma can, in fact, lead to a better anticancer treatment effect.

Accordingly, none of the cited references teach or suggest the use of flour and a sweetener in a dry flowable powder composition, and such compositions are clinically distinct from the compositions provided by the cited references. As noted in the Maurer Declaration, a composition directed to an embodiment recited in the pending claims was awarded the Eurand Award as Best New Oral Drug Formulation of 2004 by the international Controlled Release Society. Additionally, this formulation was one of three semi-finalists and eventually won the Grand Prize at the 2004 Controlled Release Society Annual Meeting. Thus, not only are the compositions of the present invention neither taught nor suggested by the cited references, these compositions fulfill a long-felt need for providing effective treatment for childhood cancers.

At least in view of the foregoing, Applicants respectfully submit that claims 2-9, 13 and 15-23 are patentable over the cited references, and Applicants respectfully request that the claim rejections under 35 U.S.C. § 103(a) be withdrawn.

## CONCLUSION

Accordingly, Applicants respectfully submit that the present application is in condition for allowance and the same is earnestly solicited. The Examiner is encouraged to telephone the undersigned at 919-854-1400 for resolution of any outstanding issues.

Respectfully submitted,

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**CERTIFICATION OF TRANSMISSION**

I hereby certify that this correspondence is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) to the U.S. Patent and Trademark Office on January 27, 2010.

Betty-Lou Rosser
Date: January 27, 2010